PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
CPW/20632		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/02557	13.06.2003	14.06.2002
International Patent Classification (IPC) or both national classification and IPC		
A61K31/55		
Applicant		
CIPLA LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07.01.2004	26.08.2004
Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Vandenbogaerde, A Telephone No. +49 89 2399-7874

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/02557

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-16 as originally filed

Claims, Numbers

1-50 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 46-47,49-50 with respect to industrial applicability

because:

☒ the said international application, or the said claims Nos. 46-47,49-50 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	/
	No:	Claims	1-50
Inventive step (IS)	Yes:	Claims	/
	No:	Claims	1-50
Industrial applicability (IA)	Yes:	Claims	1-45, 48: YES / 46-47,49-50: see separate sheet
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 46-47 and 49-50 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 97 01337 A (MCNEIL PPC INC) 16 January 1997 (1997-01-16)

D2: EP-A-0 780 127 (PROCTER & GAMBLE) 25 June 1997 (1997-06-25)

D3: DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; 2000 PORTMANN D ET AL: '[Acceptability of local treatment of allergic rhinitis with a combination of a corticoid (beclomethasone) and an antihistaminic (azelastine)]' Database accession no. NLM11233712 XP002252974 & REVUE DE LARYNGOLOGIE - OTOLOGIE - RHINOLOGIE. FRANCE 2000, vol. 121, no. 4, 2000, pages 273-279, ISSN: 0035-1334

D4: BUSSE W W ET AL: 'CORTICOSTEROID-SPARING EFFECT OF AZELASTINE IN THE MANAGEMENT OF BRONCHIAL ASTHMA' AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, AMERICAN LUNG ASSOCIATION, NEW YORK, NY, US, vol. 153, no. 1, 1996, pages 122-127, XP000604179

- D1 discloses (cf. page 2 line 8 - page 8 line 25) a combination of (i) a topical nasal antihistaminic, i.e. levocabastine, azelastine or azatadine, and (ii) a topical nasal steroid, i.e. beclomethasone, flunisolide, triamcinolone, dexamethasone or budesonide, as nasal spray or nasal drops for the treatment of allergic rhinitis.
- D2 describes (cf. page 2 line 34 - page 5 line 30, example 3) a combination of (i) an antihistamine possessing leukotriene inhibiting properties, i.e. cetirizine, loratadine or azelastine, and (ii) a glucocorticoid, i.e. beclomethasone, flunisolide, triamcinolone, fluticasone, mometasone or budesonide, as nasal

spray for the treatment of allergic rhinoconjunctivitis.

- D3 discloses (cf. abstract) a combination of (i) the antihistamine azelastine and (ii) the corticoid beclomethasone as nasal spray for the local treatment of seasonal or aperiodic rhinitis.
- D4 describes (page 126-127, discussion) that the combined use of (i) azelastine and (ii) corticosteroid medication in patients with asthma allowed patients to achieve a reduction in the use of inhaled corticosteroids while showing improvements in the severity of asthma symptoms and in pulmonary function.

V.1 Claims 1-43 - *Composition (for use in medicine)*: Novelty - Inventive step

V.1.1 The subject-matter of claims 1-43 relates to a composition per se or to a composition for use in medicine comprising (i) azelastine and (ii) a steroid, i.e. beclomethasone, mometasone, fluticasone, budesonide or cyclosenide.

V.1.2 The subject-matter of independent claim 1 is not novel according to Article 33(2) PCT over the teaching of D1, D2, D3 or D4.

V.1.3 Dependent claims 2-22 and 25 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, the reasons being as follows: Document D1, which is considered to represent the most relevant state of the art, discloses (cf. page 2 line 8 - page 8 line 25) a combination of (i) a topical nasal antihistaminic, i.e. levocabastine, azelastine or azatadine, and (ii) a topical nasal steroid, i.e. beclomethasone, flunisolide, triamcinolone, dexamethasone or budesonide, as nasal spray or nasal drops for the treatment of allergic rhinitis. The problem to be solved by the present invention may therefore be regarded as the provision of alternative formulation comprising (i) azelastine and (ii) a steroid for the treatment of allergic disorders of eye and nose or airway disorders. It would be obvious to use an alternative steroid, to use alternative carriers or to prepare an alternative formulation (i.e. inhalation formulation), because no unexpected technical effect can be seen.

V.1.4 The same objections also apply to independent claims 23 (and dependent claims 24-25), 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42 and 44.

V.2 Claims 46-50 - *Therapeutical application*: Novelty - Inventive step

V.2.1 The subject-matter of claims relates to the therapeutical application of a composition comprising (i) azelastine and (ii) a steroid, i.e. beclomethasone,

mometasone, fluticasone, budesonide or cyclosenide for the treatment of conditions for which administration of one or more anti-histamine and/or one or more steroid is indicated, i.e. irritation or disorders of the nose or eye (e.g. allergic rhinitis, rhinoconjunctivis), or airway disorders (e.g. asthma).

V.2.2 The subject-matter of claims 46-50 is not novel according to Article 33(2) PCT and/or cannot be considered as involving an inventive step in the sense of Article 33(3) PCT for the same reasons as given under point V.1.

V.3 Claims 44-45 - *Process*: Novelty - Inventive step

V.3.1 The subject-matter of claims 44-45 relates to a process for preparing a pharmaceutical composition comprising (i) azelastine and (ii) a steroid, i.e. beclomethasone, mometasone, fluticasone, budesonide or cyclosenide.

V.3.2 The subject-matter of claims 46-50 is not novel according to Article 33(2) PCT and/or cannot be considered as involving an inventive step in the sense of Article 33(3) PCT, since merely standard processes are used for preparing a composition which is already known (cf. point V.1).

V.4 Industrial applicability

For the assessment of the present claims 46-47 and 49-50 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.